REMARKS

Claims 126 and 128-145 were pending in the present application and Applicants do not make any amendment to these claims. Therefore, claims 126 and 128-145 will be under examination.

CLAIM REJECTION UNDER 35 U.S.C. §102(b)

Claims 126 and 128-145 stand rejected under 35 U.S.C. §102(b) for allegedly being anticipated by Singer et al., U.S. Patent No. 6,365,574 ("Singer").

Applicants respectfully disagree with this rejection in view of the November 8, 2006 decision by the Board of Patent Appeals and Interferences in a related case, Patent Interference 105,366 (McK). The Board held that there is "no interference-in-fact" between the claims on "substantially pure azithromycin monohydrate hemi-ethanol solvate" and the claims in Singer and its reissue application. For your convenience, a copy of the Board's decision in Patent Interference 105,366 (McK) is enclosed.

The Board had also determined that the claims of Singer and its reissue application do not anticipate or render obvious claims on "substantially pure azithromycin monohydrate hemi-ethanol solvate." The claims of the present application are directed to "pharmaceutical tablet comprising substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate and a pharmaceutically acceptable carrier or diluents." Applicants respectfully submit that Singer does not anticipate any of the pending claims. Therefore, reconsideration and withdrawal of this ground of rejection are respectfully requested.

CONCLUSION

In view of the remarks, further and favorable consideration of all pending claims are respectfully requested.

It is believed that no fee is deemed necessary in connection with the filing of the present Response. However, if any fees are required, the Commissioner is hereby authorized to charge any such fees to our Deposit Account No. 16-1445.

Respectfully submitted,

Date: November 15, 2006

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Paper 71
Entered: November 8, 2006

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE DIRECTOR OF THE
PATENT AND TRADEMARK OFFICE

ZHENG J. **LI**, ANDREW W. TRASK and JOSEPH E. MERTZ,

Junior Party
(Application 10/652,655 and
Application 10/650,252),

v.

CLAUDE **SINGER** and JUDITH ARONHIME,

Senior Party
(Patent 6,365,574 and
Application 10/816,376).

Patent Interference 105,366 (McK)
Technology Center 1600

Before: McKELVEY, *Senior Administrative Patent Judge*, and DELMENDO and LANE, *Administrative Patent Judges*.

McKELVEY, *Senior Administrative Patent Judge*.

MEMORANDUM OPINION and ORDER
Decision on Motions

A. Introduction

An interference was declared on 16 December 2005 (Paper 1). 35 U.S.C. § 135(a); 37 CFR § 41.203(a) (2005).

The proceeding is before us for consideration of motions.

Oral argument took place on 11 October 2006.

Oral argument was transcribed and a transcript of oral argument has been placed in the record. Ex 1106. References to the transcript are by page and line, *e.g.*, page 17:1-3 means page 17, lines 1-3.

B. Findings of fact

The following findings are believed to be supported by a preponderance of the evidence. To the extent that these findings discuss issues of law, they may be treated as such. Additional findings appear as necessary in the Discussion portion of this opinion.

The junior party

The junior party is Zheng J. Li [pronounced "Lie"], Andrew V. Trask and Joseph E. Mertz.

The junior party is involved on the basis of:

(1) application 10/652,655, filed 28 August 2003 and

(2) application 10/650,252, filed 27 August 2003.

The junior party has been accorded a constructive reduction to practice, *i.e.*, benefit for the purpose of priority of:

(3) application 10/152,106, filed 21 May 2002, now U.S. Patent 6,977,243, granted 20 December 2005.

The real party in interest is Pfizer, Inc.

The senior party

The senior party is Claude Singer and Judith Aronhime.

The senior party is involved on the basis of:

(1) U.S. Patent 6,365,574 B2, granted 02 April 2002, based on application 09/451,738, filed 30 November 1999 and

(2) application 10/816,376 filed 02 April 2004, seeking to reissue U.S. patent 6,365,574 B2.

The real party in interest is Teva Pharmaceutical Industries, Ltd.

The count

There is one count. Count 1 reads (Paper 1, page 9):

A composition of matter in accordance with claim 124 of Li application 10/652,655

or

a composition of matter in accordance with claim 87 of Li application 10/650,252

or

a composition of matter in accordance with claim 1 of Singer application 10/816,376.

Li claim 124

Li claim 124 reads (Ex 2006, page 1):

A crystalline form of azithromycin, wherein said form is substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate.

Li claim 87

Li claim 87 reads (Ex 2006, page 3):

> An azithromycin mixture comprising substantially pure azithromycin monohydrate hemi-ethanol solvate characterized as having a plurality of ^{13}C solid state NMR peaks with at least two peaks at approximately 179.5 ± 0.2 ppm and 178.64 ± 0.2 ppm and optionally less than 10% by weight of azithromycin dehydrate characterized as having at least three ^{13}C solid state NMR peaks at approximately 13.2 ppm, 11.3 ppm and 7.2 ppm; wherein said substantially pure azithromycin monohydrate hemi-ethanol solvate contains less than 10% of alternative polymorphic or isomorphic crystalline forms of azithromycin by weight.

Singer claim 1

Singer claim 1 reads (Ex 2005, page 3):

> An ethanolate of azithromycin having an ethanol content of about 1.5% to about 3%.

Claims of the parties

The claims of the parties are:

Li '655	124 -142 and 144
Li '252	87 and 126-136
Singer patent	1-15
Singer application	1-7

The claims of the parties which have been designated as corresponding to Count 1 are:

Li '655	124 -142 and 144
Li '252	87 and 126-136
Singer patent	1-15
Singer application	1-7

The claims of the parties which have been designated as not corresponding to Count 1 are:

Li '655	None
Li '252	None
Singer patent	None
Singer application	None

The motions

Five (5) authorized motions were filed.

Li Motion 1

Li Motion 1 seeks entry of a judgment of no interference-in-fact. Paper 24.

Singer Opposition 1 was timely filed. Paper 46.

Li Reply 1 was timely filed. Paper 57.

Singer Responsive Motion 1

Singer Responsive Motion 1 seeks leave to add proposed claims 41-43 to the involved Singer reissue application. Paper 33. The motion was filed in response to Li Motion 1 and sought to add additional claims in order for Singer to maintain that there is an interference-in-fact in the event Li Motion 1 is granted.

Li Opposition 1 was timely filed. Paper 48.

Singer Reply 1 was timely filed. Paper 54.

Singer Motion 2

Assuming that there is an interference-in-fact, Singer Motion 2 seeks to be accorded a constructive reduction to practice, *i.e.*, benefit for the purpose of priority, based on provisional application 60/110,298, filed 30 November 1999. Paper 26.

Singer also filed Singer Supplement to Motions 2 and 5A. Paper 38.

Li did not file an opposition.

Singer Motion 3

Assuming that there is an interference-in-fact, Singer Motion 3 seeks entry of judgment against the involved Li claims as being unpatentable for failure to comply with the written description requirement of 35 U.S.C. § 112, ¶ 1. Paper 27.

Li Opposition 3 was timely filed. Paper 49.

Singer Reply 3 was timely filed. Paper 55.

Singer Motion 5(b)

Assuming that there is an interference-in-fact, Singer Motion 5(b) seeks entry of judgment against the involved Li claims as being unpatentable over the prior art under 35 U.S.C. § 102(b) and 35 U.S.C. § 103. Paper 29.

Li Opposition 5(b) was timely filed. Paper 47.

Singer Reply 5(b) was timely filed. Paper 56.

The Li invention

The Li invention relates to crystal forms of azithromycin. Ex 2003, page 1, line 3 and page 2, line 4.

According to Li, azithromycin is sold commercially and is an effective antibiotic in the treatment of a broad range of bacterial infections. Ex 2003, page 1, lines 3-5.

A "crystal form" or "form" means one or more crystal forms of azithromycin. Ex 2003, page 2, lines 5-6.

Several "crystal forms" of azithromycin are described in the Li specification.

The crystal form of general interest in this interference is what Li, acting as its own lexicographer, calls "Form F."

More particularly, Li describes an embodiment which it identifies as "substantially pure" Form F.

Two forms of azithromycin were known prior to Form F: Form A and Form B. Ex 2003, page 9, lines 21-23.

Sixteen other forms are said to have been discovered. Ex 2003, page 9, lines 23-24.

Form F azithromycin has the empirical chemical formula:

$$C_{38}H_{72}N_2O_{12}\cdot H_2O\cdot 0.5C_2H_5OH$$

in the single crystal structure and is known as azithromycin monohydrate hemi-ethanol solvate. Ex 2006, page 2, line 14. The structural chemical formula of azithromycin can be found at Ex 2003, page 1, line 8.

Form F is said to be further characterized as containing 2-5% water and 1-4% ethanol by weight in powder samples and having a powder X-ray diffraction 2Θ peaks as defined in Table 9. Ex 2006, page 2, lines 15-17.

The ^{13}C ssNMR (solid state Nuclear Magnetic Resonance) spectrum of Form F is said to have two chemical shift peaks at approximately 179.5 ± 0.2 ppm and 178.6 ± 0.2 ppm, a set of five peaks between 6.4 to 11.0 ppm, and ethanol peaks at 58.0 ± 0.5 ppm and 17.2 ± 0.5 ppm. The solvent peaks can be broad and relatively weak in intensity. Ex 2003, page 2, lines 17-21.

The described invention also relates to "substantially pure" Form F and methods of making substantially pure Form F azithromycin. Ex 2003, page 2, lines 22 and 27-28; Ex 1006, page 17:7-13. It is the "substantially pure" Form F which is now claimed by Li.

The term "substantially pure" is defined in the Li specification, when referring to a designated crystalline form of azithromycin, to mean that the designated crystalline form contains less that 20% (by weight) of residual components such as alternate polymorphic or isomorphic crystalline forms of azithromycin. Ex 2003, page 5, lines 22-25.

Li tells us that it is *preferred* that a substantially pure form of azithromycin contains less than 10% (by weight) of alternate polymorphic or isomorphic crystalline forms of azithromycin, *more preferred* less than 5% (by weight) of alternate polymorphic or isomorphic crystalline forms of azithromycin, and *most preferably* less than 1% (by weight) of alternate polymorphic or isomorphic crystalline forms of azithromycin. Ex 2003, page 5, lines 25-29.

Li does not explicitly explain the scientific basis for the "preferred", "more preferred" and "most preferably" percentages.

Fig. 10 of the Li application is said to be an experimental powder X-ray diffraction pattern of azithromycin Form F. The scale of the abscissa

(x-axis) is in degrees 2-theta (2 Θ). The ordinate (y-axis) is the intensity in counts. Ex 2006, page 8, lines 9-10.

Crystallographic data of azithromycin Form F is set out in Table 5. Ex 2003, pages 11-12. *See also* Ex 1105, page 25:1-16 (Meenan cross examination).

The single crystal of Form F is described as being crystallized in a monoclinic space group, $P2_1$, with an asymmetric unit containing two azithromycin molecules, two water molecules and one ethanol molecule, as a monohydrate/hemi-ethanolate. Ex 2003, page 14, lines 34-36.

Form F is isomorphic to all family I azithromycin crystalline forms. Ex 2003, page 14, lines 36-37.

Family I isomorphs are identified as hydrates and/or solvates of azithromycin where the solvent molecules in the cavities have a tendency to exchange between solvent and water under certain conditions. Ex 2003, page 17, lines 32-34.

Therefore the solvent/water conditions of the isomorphs may vary. Ex 2003, page 17, lines 34-35.

The theoretical *water* content of a single crystal of Form F is 2.3%. The theoretical *ethanol* content (rounded to one decimal place) of a single crystal of Form F is 2.9%. Ex 2003, page 15, line 1. *See also* Ex 2009, fifth page, ¶ 4[1] and Ex 1105, page 26:15-18.

The powder samples of Form F are said to show a dehydration/desolvation endotherm at an onset temperature between 110-125°C. Ex 2003, page 15, lines 1-3. At the endotherm, any water of

[1] We note that Dr. Quallich's "prior declaration" is inadvertently identified as Ex 1009 at Ex 2007, ¶ 9, line 3. We understand the reference to Ex 1009 to be a reference to Ex 2009.

hydration and any ethanol bound in the crystal will begin to separate from any azithromycin molecules.

In general, Form F is prepared by dissolving azithromycin in ethanol (1-3 volumes by weight) at a temperature of about 50-70°C. Upon complete dissolution, the solution is cooled to subambient temperature to cause precipitation. The volume of ethanol can be reduced by vacuum distillation with stirring for 1-2 hours to increase the yield. Ex 2003, page 15, lines 3-6.

Water (optionally chilled to 0-20°C) in an amount of about 0.1-2 volume can be added with collection of solids within 30 minutes after water addition. Cooling the ethanol solution of azithromycin prior to the addition of water to below 20°C, *preferably* below 15°C, *more preferably* below 10°C, and *most preferably* 5°C results in "substantially pure" azithromycin Form F. The solid Form F azithromycin is collected by filtration and dried. Ex 2003, page 15, lines 6-11.

Example 2 describes the preparation of Form F. In Example 2A, which we understand to be based on actual experimentation (Ex 1106, page 23:5-7), azithromycin dihydrate was slowly added to one volume of warm ethanol at about 70°C, and stirred to complete dissolution at 65 to 70°C. The resulting solution was allowed to cool gradually to 2-5°C and one volume of chilled water was added. The crystalline solids were collected shortly (preferably less than 30 minutes) after addition of water by vacuum filtration. Ex 2003, page 18, lines 18-21.

In Example 2B, which we understand may be prophetic (Ex 1106, page 23:6-7), azithromycin dehydrate is slowly added to one volume of warm ethanol at about 70°C, and stirred to complete dissolution at 65 to 70°C. The solution is allowed to cool gradually to 2-5°C and ethanol

volume may be reduced by vacuum distillation. Seeds of Form F 1-2% wt may be introduced to facilitate the crystallization. After stirring up to 2 hours the crystalline solids are collected by vacuum filtration. The isolation of the crystals is said to yield "substantially pure" Form F azithromycin, Form F azithromycin substantially free of Form G azithromycin and Form F azithromycin substantially free of azithromycin dihydrate. Ex 2003, page 18, lines 22-28.

The Singer invention

The Singer invention relates to what Singer calls "a new ethanolate of azithromycin." Ex 2001, col. 1, lines10-11.

According to Singer, the new ethanolate is less "hygroscopic" than azithromycin monohydrate. Ex 2001, col. 1, lines 61-63 and col. 2, lines 23-25.

A hygroscopic substance has the property of adsorbing moisture from the air. A common example of a hygroscopic substance is silica commonly found in bags in many products sold in commerce when it is desirable to keep the product free of moisture, *e.g.*, electronic gear and pharmaceuticals including aspirin.

Singer's new ethanolate is said to be less inclined to adsorb water than azithromycin monohydrate. *See* Fig. 1 for what Singer says is a comparison of water uptake of a representative new ethanolate vis-à-vis azithromycin monohydrate. Ex 2001, col. 2, lines 29-31. We do not know precisely how the new ethanolate used to generate the data in Fig. 1 was made. Nor did Li's witness Dr. Paul Meenan. Ex 1105, page 44:14-15 and pages 45:16 through 46:4.

The new ethanolate is said to have ethanol and water contents as follows:

Component	Broad Range	Preferred Range
Ethanol	about 1.5 to about 3	about 1.5 to about 2.5
Water	about 2 to about 4	about 2.5 to about 3.5

Ex 2001, col. 1, lines 63-64 and col. 2, lines 25-28.

Singer does not provide a scientific explanation for the preferred range vis-à-vis the broad range. Nor does Singer explicitly state whether ethanol content includes both ethanol bound in a crystal lattice and ethanol adsorbed on the lattice. Ethanol measurements are said to have been made by gas chromatography. Ex 2001, col. 2, line 67 and col. 3, lines 5-6. Our understanding is that an ethanol measurement made by gas chromatography would measure both bound and unbound ethanol. *See also* Ex 1106, page 7:9-14.

A general method for making the new ethanolate is described as follows. Azithromycin is dissolved in absolute ethanol, in a ratio of about 2.5:1 (ethanol:azithromycin by weight) at a temperature of between about 10°C and about 80°C, *preferably* at about 20°C to about 30°C. A minimal amount of water is added, *i.e.*, an amount to greater than 20% (by weight versus ethanol), *preferably* about 6 to about 16%. The solution is heated slowly at a constant temperature gradient over a first time interval of about 2 to about 18 hours, *preferably* about 3 to about 8 hours, reaching a maximum temperature of about 30°C to about 80°C, *preferably* about 40°C to about 60°C at the end of the first time interval. Crystallization appears to begin in the temperature range of about 30-45°C. During the first time interval, the

water content of the solution is gradually increased, but a concentration of no more than about 50%. Ex 2001, col. 2, lines 38-53.

At the end of the first time interval, the resulting suspension is maintained at the maximum temperature for a second time interval of about 1 to about 18 hours, *preferably* about 1 to about 4 hours. During the second time interval, additional water is added to complete the crystallization process. Ex 2001, col. 1, lines 54-59.

At the end of the second time interval, the suspension is cooled using a constant temperature gradient over a third time interval of about 1 to about 18 hours, *preferably* about 2 to about 4 hours, reaching a final temperature of about 20°C. A resulting precipitate is collected by filtration and dried to a constant weight. Ex 2001, col. 2, lines 60-65.

Singer does not provide any scientific bases or analysis for its various "preferably" options.

In an example, Singer describes making the new ethanolate as follows. Ten grams of azithromycin crude was introduced into a 0.25 liter three-necked flat flanged jacketed vessel equipped with a mechanical stirrer, a condenser and thermometer and containing 30 ml of absolute ethanol at 20°C. Three ml of water at 20°C were added and the solution was heated at a constant temperature gradient so as to reach 55°C after 4 hours. Between 35°C and 55°C, additional water having a total volume of 11 ml was slowly added at regular time intervals. When 55°C was reached, the resulting suspension was maintained at 55°C for 2 hours, during which an additional 49 ml of water was added. The suspension was then cooled from 55°C to 20°C over 2 hours. A precipitate was filtered. After drying, 9 g of

azithromycin ethanolate were obtained. Ex 2001, col. 3, line 54 through col. 4, line 6.

Table 1 in the Singer specification shows the water content and ethanol content (% weight/weight) of various batches of the new ethanolate, *i.e.*, Batches A through G.

Batch	Ethanol Content	Water Content
A	2.2	3.24
B	2.3	2.46
C	2.2	2.71
D	2.3	2.77
E	2.2	3.28
F	1.52	2.70
G	1.7	3.40

We were told at oral argument (Ex 1106, page 51:5 through 52:22), and the Singer specification suggests (Ex 2001, col. 2, lines 38-67), that Batches A through G were made using the process generally described at col. 2, lines 35-67 of the Singer patent. But, we do not know the precise process parameters used to each batch. Ex 1106, page 14:14-21.

Since different process parameters may have been used to make each batch, then based on the water contents and ethanol contents reported in Table 1, it becomes manifest that the water content and ethanol content are a function of process parameters, *e.g.*, (1) temperature at which azithromycin is dissolved in ethanol (10°C to 80°C), (2) amount of water (no greater than 20%, preferably about 6% to about 16%), (3) slow heating (about 2 hours to about 18 hours), (4) suspension heating time interval (about 1 hours to about 18 hours, preferably about 2 to about 4 hours), (5) drying temperature and (6) perhaps other parameters. Ex 1106, page 53:1-20.

Additionally, we note that the specification does not discuss any "error rate" for ethanol and water content measurements.

To repeat the process and obtain, *e.g.*, Batch A, one skilled in the art would have to vary the parameters in one or more experiments until a water content of 3.24% and an ethanol content of 2.2% is obtained, because explicit directions are not given as to how each Batch was prepared.

What is said to be a characteristic powder X-ray diffraction pattern of an azithromycin ethanolate of the invention is shown in Fig. 2. Ex 2001, col. 2, lines 29-31. The reader needs to note that two-theta values in Fig. 2 increase from right to left, whereas in Li Fig. 10 the two-theta values increase from left to right.

The specification does not explicitly state which sample (e.g., Batch A through G or the Example or some other unidentified sample) was used to obtain a powder X-ray diffraction pattern.

The record suggests that the diffraction pattern may have come from an analysis of a sample from a lot identified as Lot #SC-311 (Ex 1106, page 21:11 through page 22:2 and page 74:10-14), but Lot #SC-311 *per se* and a process for making Lot #SC-311 are not explicitly identified in the Singer patent. Ex 1020, ¶ 2-3; Ex 1066.

Testimony of George Quallich

Dr. George J. Quallich testified on behalf of Li.

Dr. Quallich has been qualified as an expert, *inter alia*, in the field of crystallization of pharmaceutical compounds. Ex 2007, ¶ 1 and Ex 2008.

Dr. Quallich was asked to provide an opinion as to what is meant by the term "substantially pure" as used in the specification and claims of the involved Li applications.

While the meaning of a phrase in a claim raises a question of law, nevertheless Dr. Quallich discusses certain factual matters, with reference to the Li specification, which we find to be useful.

Dr. Quallich points out that the Li specification describes both (1) single crystals and (2) powder samples. Ex 2007, ¶ 8.

Dr. Quallich explains that a single crystal of azithromycin Form F is exactly that—a single crystal.

Another term used in the interference is a "bulk" sample which is a complete batch of crystalline product recovered by recrystallization—not a single crystal. Ex 2007, ¶ 11.

A powder sample is made by grinding to a powder a bulk sample recovered by recrystallization. Ex 2007, ¶ 12, second sentence.

Dr. Quallich acknowledges that the Li specification states that the ethanol content of a Form F can range from 1% to 4%. Ex 2007, ¶ 12; Ex 2003, page 2, lines 15-16.

Dr. Quallich also explains that the theoretical amount of ethanol in a single crystal is 2.9% (rounded to one decimal place). Ex 2007, ¶ 12. *See also* Ex 2003, page 15, line 1 and Ex 1105, page 26:15-18.

To the extent that the Li specification describes an ethanol content range of 1-4% for Form F, Dr. Quallich tells us that the "range" refers to the powder and not a single crystal which can only have a maximum of 2.9% ethanol. Ex 2007, ¶ 12; *see also* Ex 2003, page 15, line 1.

The powder, however, can contain both (1) bound ethanol in crystal lattices therein and (2) absorbed ethanol on the surface of those crystals lattices. Ex 2007, ¶ 12.

Dr. Quallich illustrates his point by reference to Ex 2010, which appears below where it can be plainly seen that the powder sample can be

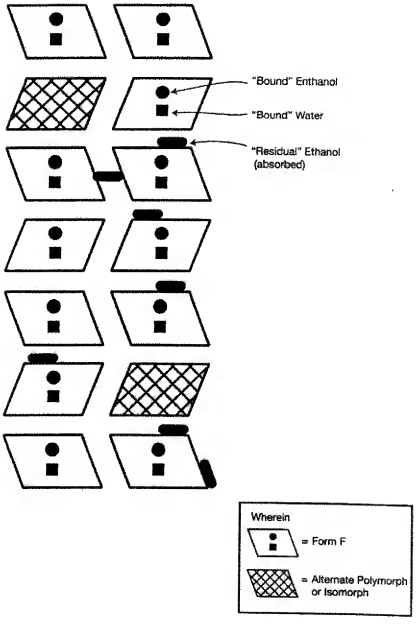
made up, *inter alia*, of (1) single Form F crystals, (2) single polymorphic or isomorphic crystals and (3) absorbed or residual ethanol. Ex 2007, ¶ 12 and ¶ 17.

Ex 2010 illustrates a bulk or powder sample having (a) 12 Form F crystals each containing ethanol, (b) 2 polymorphic or isomorphic crystals, e.g., azithromycin dihydrate, and (c) 7 absorbed molecules of ethanol. Ex 2007, ¶ 17.

Based on his testimony, we believe that that the "illustrative" powder mix shown in Ex 2010 is "substantially pure" because it contains only 14.2% [(2/14) x 100] of "residual component such as alternate polymorphic or isomorphic crystalline form(s) of azithromycin" (quote from the Li specification, Ex 2003, page 2, lines 23-25).

Dr. Quallich also point out, correctly we believe, that an ethanol content of 1% is inconsistent with a claim to "substantially pure" Form F, which must have 2.91% (rounded to two decimal places) ethanol. *See* Ex 2007, ¶ 12. See also testimony by Li's witness Dr. Meenan. Ex 1105, page 26:6-10 and page 56:15-18.

Exhibit 2010



1

Dr. Quallich explains that a sample having less than 2.9% ethanol cannot consist of 100% Form F single crystals. Ex 2007, ¶ 15.

Dr. Quallich acknowledges that the Singer patent describes ethanol and water contents in azithromycin ethanolates identified in Table 1 (Ex 2001, col. 3) as Batches A through G. Ex 2007, ¶ 36.

Dr. Quallich has provided results of calculations which show the weight percent of azithromycin monohydrate hemi-ethanolate in Batches A through G. Those percentages run from as low as 52.22% (Batch F) to as high as 79.01 (Batches B and D). Ex 2009, ¶ 6.

On the basis of the calculations, Dr. Quallich explains that none of the azithromycin ethanolates of Batches A through G can be "substantially pure" Form F because none have 80% or more azithromycin monohydrate hemi-ethanolate. Ex 2007, ¶¶ 36-38.

Testimony of Robin Rogers

Dr. Robin D. Rogers testified on behalf of Singer. Ex 1097. *See also* Ex 1045.

Dr. Rogers has been qualified as an expert, *inter alia*, in the field of crystal engineering, X-ray crystallography, crystallization and polymorphism. Ex 1097, ¶ 3.

Dr. Rogers indicates that a reference to a "single crystal" is a reference to an "individual crystal." Ex 1097, ¶ 13. In this respect, Dr. Rogers appears to agree with Dr. Quallich.

Dr. Rogers also indicates that he understands "bulk" to refer to the product of a crystallization process and would contain many single crystals. Ex 1097, ¶ 14. In this respect, Dr. Rogers again appears to agree with Dr. Quallich.

Based in part on his reading of the specification, including Li application original claims 1, 8 and 9, Dr. Rogers testifies that one having ordinary skill in the art would understand that "substantially pure" Form F could have from 1-5% ethanol. Ex 1097, ¶ 24.

Original claim 1 of the Li application reads (emphasis added):

> 1. A crystalline form of azithromycin selected from the group consisting of forms D, E, *substantially pure* F, G, J, M substantially in the absence of azithromycin dihydrate, N, O, P, Q and R.

Original claim 8 of the Li application reads:

> 8. A crystalline form of azithromycin according to claim 1 wherein said form is substantially pure form F.

Note that claims 1 and 8 state "substantially pure [Form] F" (a subgenus) not just "[Form] F" (a genus). Thus, it will be observed from the outset that Li limited the Form F claim coverage to "substantially pure" Form F.

Original claim 9 of the Li application reads:

> 9. A crystalline form according to claim 8 wherein said form is characterized as containing 2-5% water and 1-5% ethanol by weight in a powder sample.

Dr. Rogers expresses disagreement with a conclusion reached by Dr. Quallich that a sample with less than 2.9% ethanol cannot be pure Form F. Ex 1097, ¶¶ 25-26.

The basis for Dr. Rogers' disagreement seems to be a statement in the Li specification to the effect that "Form F is further characterized as containing 2-5% water and 1-4% ethanol in powder samples." The sentence in the Li specification to which Dr. Rogers makes reference discusses Form F, not "substantially pure" Form F. Ex 2003, page 2, lines 15-16. In the paragraph which follows, Li states that "[t]he invention *also* relates to substantially pure [F]orm F azithromycin ***." (Emphasis added). Ex 2003, page 2, line 22.

Dr. Rogers mentions claim 9 in support of his disagreement with Dr. Quallich.

We have some misgivings as to (1) whether claim 9 was ever a viable claim (35 U.S.C. § 112—enablement), (2) whether it is a proper dependent claim (35 U.S.C. § 112 (fourth paragraph) (Ex 1106, page 18:19-21) and (3) whether it can reliably serve as a basis for rendering opinions on what one skilled in the art would understand "substantially pure" to mean. We are not aware of any description in the Li application which would enable a person having ordinary skill in the art to make a "substantially pure" Form F having 1% ethanol. For example, Dr. Meenan convincingly testified that substantially pure Form F cannot have a 1% ethanol content. Ex 1105, page 56:15-18. Dr. Quallich gave similar convincing testimony. Ex 2007, ¶ 16. Moreover, it would appear that claim 9 may have sought to improperly enlarge the scope of the claims from which it depended (claim 8) by enlarging the percent of ethanol which can be present in the "substantially pure" Form F. A claim which is not a proper claim and which probably expresses a scientific impossibility is hardly a reliable basis upon which to assess the meaning of "substantially pure."

Dr. Rogers expresses an opinion that the Singer application describes "substantially pure" Form F, specifically that Singer's "azithromycin ethanolate" is the same crystalline form as Li's "substantially pure azithromycin monohydrate hemi-ethanol solvate." Ex 1097, ¶ 38.

In support of his opinion, Dr. Rogers considered the PXRD (powder X-ray diffraction) of Fig. 2 of the Singer patent. Ex 1097, ¶¶ 40-41. However, all Singer says with respect to Fig. 2 is that it "is a characteristic powder X-ray diffraction pattern of the azithromycin ethanolate of the present invention." Ex 2001, col. 2, lines 17-18. The Singer patent does not identify the specific azithromycin ethanolate from which the PXRD pattern was generated.

Dr. Rogers also notes that the Singer azithromycin ethanolate can have from 1.5% to 3% ethanol content (Ex 2001, col. 2, lines 25-26), which in Dr. Rogers' opinion "is essentially the same" as the 1% to 4% ethanol content described by Li. Ex 1097, ¶ 42. However, Dr. Rogers does not explain how "substantially pure" Form F can have 1% ethanol.

Dr. Rogers also considered data reported as a result of the experiment conducted by Dr. Perlman, an experiment discussed later in this opinion. Ex 1097, ¶¶ 44-47.

Based on the data, Dr. Rogers concludes that Dr. Perlman's NP-P5 is "substantially pure" Form F as defined by Li. Ex 1097, ¶ 48.

Dr. Rogers opinions are based on data supplied to him by Teva and thus stand or fall with the reliability of Dr. Perlman's experimental work.

Rebuttal testimony of Dr. Paul Meenan

Dr. Paul Meenan testified as a rebuttal witness on behalf of Li.

Dr. Meenan has been qualified as an expert, *inter alia*, in the field of crystallization, solid-state simulation and powder technology. Ex 2051, ¶ 1 and Ex 1105, *e.g.*, page 5:10-15 and page 17:20-22.[2]

When asked to express an opinion, Dr. Meenan testified that an ethanol content of a Singer azithromycin ethanolate having "about 1.5 to about 3%" ethanol would be understood as referring to total ethanol content, both bound and unbound ethanol. Ex. 2051, ¶ 3.

Agreeing with Dr. Quallich, Dr. Meenan testifies that for a single Form F crystal, any ethanol in excess of 2.91% would be unbound or absorbed ethanol. Ex 2051, ¶ 7.

Dr. Meenan expresses a difference of opinion with Dr. Rogers on whether "drying to constant weight would remove any 'unbound' ethanol." Ex 2051, ¶ 8.

Dr. Meenan suggests that the water and ethanol contents of Batches A through G (assuming they were actually made) may not have been dried to constant weight prior to any water and ethanol content analysis. Ex 2051, ¶ 12.

Dr. Meenan also expresses a disagreement with Dr. Rogers concerning whether drying to constant weight would remove all "unbound" ethanol, again relying on ethanol and water content data from Batches A

[2] Ex 1105 is a transcript of the cross examination deposition of Dr. Meenan. It has two sets of page numbers: (1) one at the bottom designated as "Page n" where "n" is the page number and (2) other page numbers in the body of the transcript. The lines are numbered, but the top line on any given Page n is not line 1. In this opinion, we refer to "Page n" followed by the line numbers, e.g., page 5, lines 20-6. Note that the second numbered line (6) may be a number less than the first numbered line (20).

through G. Ex 2051, ¶¶ 15-19. We find the analysis based on the Table in ¶ 17 and the discussion in ¶ 18 persuasive.[3]

Singer cross examined Dr. Meenan. Ex 1053.

Dr. Meenan testified that it would be his view that a sample should be dried before subjecting the same to water content analysis via a Karl Fischer water analysis, explaining that drying is necessary to achieve consistency. Ex 2051, page 12:20-23. Singer's point apparently is that if Dr. Meenan would dry before analysis why would Singer not also have dried before analysis. The answer was provided in Dr. Meenan's direct testimony—the results reported in water content for Batches A through G are not consistent.

Singer attempted on cross examination to get Dr. Meenan to say that how one viewed the Singer disclosure depending on whether the ethanol content was calculated to zero, one or two decimal places. Ex 2051, page 25:23 through page 30:2. The objective apparently was to get Dr. Meenan to agree that if calculations were made to "zero" decimal points, then a calculation resulting in a "3" would be "about 3" fall within the range of "about 1% to about 3%" ethanol content described by Singer. Dr. Meehan "personally wouldn't" round 2.9 up to 3. Ex 2051, page 30, line 2; Ex 1106, page 8:14-17 and page 76:4-10. Dr. Meenan's explanation speaks for itself and we would be hard pressed to disagree with his explanation. So like Dr. Meenan, we likewise decline to round 2.9 up to 3.

Dr. Rogers testified that "2.3" could be any number from 2.251 through 2.349. Ex 1045, ¶ 59; Ex 1106, pages 11:18 through 12:3. But, the

[3] We have some concern with respect to the statement "(for example, for Batch A, the value is 75.5% of 2.27, or 1.7365)." We are not entirely sure of the basis for the number 2.27, since the Singer patent states a number of 2.2. Our concern is not significant, however, because Batches B and D have an ethanol content of 79%, which is closer to Li's required 80% than either a 75.5% or 75.6% of Batch A.

number in the Singer patent is 2.3. To the extent that one might speculate, as Dr. Rogers suggests, that 2.3 is 2.349 it is just as reasonable to find that it means 2.251. Inherency cannot be established on the basis of speculation.

Dr. Meenan testified that for a hygroscopic material, a water content analysis could be a function of the time when you measured water content because a material could pick up water if a measurement is not made shortly after drying. Ex 1105, page 40:13-11 and page 48:17 through page 50:15.

At the end of cross examination, the following took place. Ex 1105, page 52:18 through page 53:5.

> Q. [By Ms. Moken, counsel for Singer] Do you have any reason to believe that the inventors of the 574 patent would have lied in saying that they dried the samples to constant weight?
>
> A. [By Dr. Meenan] I would say that I disagree with their conclusions that they dried to constant weight.
>
> Q. So, you are saying that they lied when they said that they dried the samples to a constant weight?
>
> *****
>
> A. I don't think—I'm not saying that they are lying. I'm just saying that I think the data supports that the samples haven't been dried to constant weight.

The second question is somewhat troubling in light of Dr. Meenan's response to the first question. "Lying" is not the issue and probably should never have been brought up in the first place. Rather, what is apparent is that Dr. Meenan disagrees with conclusions stated by Singer in the Singer patent. An expression of a legitimate difference of opinion on a scientific

matter should not turn into an accusation or a suggestion of "lying." Dr. Meenan is firmly of the view that notwithstanding statements in the Singer patent, there is data set out in the Singer patent from which one can conclude that samples were not dried to constant weight. The line of questioning set out above in no way undermines the soundness of Dr. Meenan's position.

The Perlman reproduction of the Singer patent Example

After the interference was declared, Singer undertook a post-litigation project to reproduce the Example of its patent to show that it inherently will produce "substantially pure" Form F within the meaning of the Li claims.

Experimental work purporting to reproduce the Example was conducted under the direction of Dr. Nurit Perlman. Ex 1017, ¶ 4.

According to Dr. Perlman, a "protocol" (Ex 1033) describes the method she was to use to reproduce the Example. Ex 1017, ¶ 4.

Li cross examined Dr. Perlman. Ex 2043.

Dr. Perlman's direct declaration testimony with respect to reproducing the Example was the following. Ex 1017, ¶ 6 [matter in brackets is presented to indicate our understanding of abbreviations].

> As documented in [the protocol, which is] Exhibit 1033, on February 1, 2006, I dissolved 10.02 g [grams] azithromycin in 30 ml [milliliters] absolute ethanol at 20°C in a 0.25 L [liter] reactor equipped with a mechanical stirrer, a condenser, and a thermometer. 3 ml of water was added. The solution was heated to 55°C over 4 hours with a constant temperature gradient. Between 35°C and 53°C, 11 ml of additional water was added. The mixture was then stirred at 55°C for 2 hours,

during which time an additional 49 ml of water was added. The mixture was then cooled to 20°C over 2 hours. The precipitate formed was filtered and dried in a vacuum oven at 40°C for roughly 16 hours, yielding 6.48 [grams] of white powder.

Dr. Perlman marked the samples as NP-P5. Ex 1017, ¶ 7.

Dr. Perlman caused samples to be sent to (1) Ayelet Sherman-Gultchin, (2) Maya Cwikel and (3) Dr. Clare Grey.[4] Ex 1017, ¶ 7.

Dr. Perlman does not state how or when she gave, or otherwise sent, samples to the three individuals.

Ayelet Sherman-Gultchin testified that on February 20, 2006, she received a sample of crystalline material from Nurit Perlman marked NP-P5. Ex 1018, ¶ 5. She does not testify who actually gave her the sample.

Ms. Sherman-Gultchin generated a PXRD [powder X-ray diffractogram] spectrum for the sample. Ex 1018, ¶ 6; Ex 1046.

Maya Cwikel testified that on March 6, 2006, she received a sample of crystalline material from Dr. Perlman marked NP-P5 and analyzed the sample for ethanol content by "headspace gas chromatography". Ex 1019, ¶¶ 4-6; Ex 1034. Ms. Cwikel does not state precisely how she first received the sample.

Dr. Clare Grey testified that he received and analyzed a sample of Teva's azithromycin ethanolate Lot No. NP-P5 using CPMAS ssNMR to obtain the ssNMR spectra of the substance. Ex 1015, ¶ 17; Ex 1096, ¶ 6.

Dr. Grey does not state from whom he received the sample.

[4] Throughout the record, we have encountered different spellings for the names of these individuals. For consistency, we use the spellings in the declarations signed by the individuals on the assumption that they are most likely to know how their names are spelled.

Dr. Grey "understands" that Lot No. NP-P5 was prepared in accordance with the Singer Example, but does not state the basis for his "understanding." Ex 1015, ¶ 18.

According to Dr. Grey, the ssNMR spectrum confirms that Lot No. NP-P5 is the same compound as that of Form F of Li. 1015, ¶¶ 22-23.

Dr. Grey also testified that PXRD data confirmed that NP-P5 is the same compound as substantially pure Form F of Li. Ex 1015, ¶ 24.

Li, with candor which we find refreshing, states that Li can admit that the sample analyzed as "NP-P5"—however it was made—appears to be "substantially pure" as can be determined by a combination of ethanol content, powder X-ray diffraction, and solid state NMR. Paper 57, page 5, lines 12-14.

However, Li sees more than a few lose ends in the overall testing scheme: (1) Did Dr. Perlman follow the Example? (2) Has Singer reliably established a chain of custody of the tested samples from Dr. Perlman to Ms. Sherman-Gultchin, Ms. Cwikel and Dr. Grey?

Li's position on the Teva experimental work arises in large measure on the basis of cross examination of Dr. Perlman. Ex 2043.

In evaluating the cross examination testimony of Dr. Perlman, we have taken into account that her "first" language appears to be Hebrew. Counsel (Mr. McMorrow for Li and Mr. Lee for Singer) were able to agree without any apparent difficulty to secure the attendance at the cross examination deposition of individuals who are familiar with both English and Hebrew to help things along. Ex 2043, page 5:12 through page 6:21. Ms. Holland attended for Singer and Mr. Nissenbaum attended for Li. We commend Mr. McMorrow and Mr. Lee for the manner in which the matter was efficiently handled without any apparent controversy. Ex 1106,

page 38:19 through page 39:1. We also recognize that taking any deposition, let alone one in English of a person whose primary language is Hebrew and who may not be totally comfortable answering English-language questions, is ordinarily somewhat of a "tense" environment for a scientist, like Dr. Perlman. The record shows that both Mr. McMorrow and Mr. Lee were properly sensitive to these difficulties and the overall feeling of the witness.

The cross examination reveals that there is more to the story than the direct testimony suggests.

Mr. Benzion Dolitzky, a scientist, is Dr. Perlman's manager. Ex 2043, page 23, lines 22-25.

Dr. Perlman received from Mr. Dolitzky a "protocol" (Ex 1090) to be used in reproducing the Singer Example. Ex 2043, page 23:4-6 and page 59:23 through page 61:10 (redirect). Based on the oral argument, there is a possibility that the overall procedure may have been developed "on-the-fly." Ex 1106, page 40:18-19.

The protocol states that azithromycin is to be added to absolute ethanol. Ex 1090, page 3. Dr. Perlman's lab notebook gives the impression that azithromycin was dissolved in absolute ethanol. Ex 1033. The Example states that azithromycin is to be added to absolute ethanol. Ex 2001, col. 3, lines 56-59. During cross examination, Dr. Perlman states a belief that ethanol was added to azithromycin (in the form a powder) in the reactor. Ex 2043, page 33:8-19; Ex 1106, page 39:2-8. Based on the evidence, as a whole, we are not sure whether ethanol was added to azithromycin or whether azithromycin was added to ethanol. Nor do we know if it makes a difference.

The protocol states that the ethanol should be at 20°C before azithromycin is added. Ex 1090, page 3. Dr. Perlman's laboratory notebook identifies a "jacket" associated with the reactor: "(Jacket 20°C)". Ex 1033. The Example states that the ethanol is to be at 20°C when the azithromycin is added. Ex 2001, col. 3, line 59. When asked if she raised the temperature to 20°C before or after absolute ethanol was added, Dr. Perlman said "I don't remember." Ex 2043, page 35:6-9. Based on the record, as a whole, we cannot determine if the temperature was raised to 20°C or if it was 20°C all along. *See, e.g.*, Ex 2043, page 62:11-15.

The protocol states the temperature of the mixture is to be heated to 55°C over 4 hours and 11 ml of water added. Ex. 1090, page 3. Dr. Perlman's lab notebook states that the mixture was heated using a constant temperature gradient to 55°C and 11 ml of water was added starting when the temperature was 35°C and ending at 53°C. The Example states that 11 ml is to be slowly added at regular time intervals between 35°C to 55°C. Ex 2001, col. 3, last line to col. 4, first line. During cross examination, Dr. Perlman testified that the 11 ml was added manually and that the precise amounts and time of water addition are not recorded in her lab notebook. Ex 2043, page 38, line 25 through page 42:5. Based on the record, as a whole, we cannot determine precisely when and in what amounts water was added. Nor do we know if it makes a difference.

The protocol states that a suspension is to be maintained at 55°C for a 2 hour time period and during the period 49 ml of water is to be added. Ex 1090, page 3. Dr. Perlman's lab notebook states that the mixture was stirred at 55°C for 2 hours and during this time 49 ml of water was added.

The Example states that a suspension was maintained at 55°C for 2 hours, during which an additional 49 ml of water was added. Ex 2001, col. 4, lines 1-3. During cross examination, Dr. Perlman reveals that the 49 ml of water was added in small portions (less that 1 ml) over the 2-hours period, but she cannot remember how many portions were added or the time interval when water addition occurred. Ex 2043, page 44:21 to page 46:6. We cannot determine precisely how often, or when, small portions of water were added to the suspension. Nor do we know if it makes a difference.

The protocol states that the suspension is filtered by vacuum at 20°C and dried in a vacuum oven at 40°C. Ex 1090, page 3. Dr. Perlman's lab notebook states that vacuum filtration occurred (no temperature is set out) and vacuum dried occurred at 40°C starting at 1660 hours [sic—1640 hours] and ending at 0900 hours the next morning. The Example states that the precipitate in the suspension was filtered and dried. A drying time and a drying temperature are not set out in the Example. During cross examination, Dr. Perlman agreed that the Example did not give much information concerning filtration and drying. Ex 2043, page 48:7-15 (filtration) and page 50:12-15 (drying). Dr. Perlman testified that drying took place overnight beginning at 1640 hours and ending the next day at 0900 hours. Ex 2043, page 50:20 through 51:10. When asked how she determined the drying time given that the Example has no drying time, Dr. Perlman indicated that she dried according to the protocol. Ex 2043, page 51:12-17. Dr. Perlman also indicated that she selected 40°C as the drying temperature because it was in the protocol, albeit she did not know why 40°C was selected. Ex 2043, page 51:12 through page 52:24.

The protocol does not state an expectation of the amount of product to be obtained, but it is to be divided into 8 vials. Ex 1090, page 3. Dr. Perlman's lab notebook states that 6.48 grams of sparkling white powder was obtained and was divided into 8 tightly closed "powder" [sic "vials"]. Ex 1033, page 2; Ex 2043, page 63:10 through page 64:3. On re-direct, Dr. Perlman testified that "[a]s I remember", product was left in the reactor after taking out the 6-point something grams, but she does not say how much product was left or why all the product was not removed. Ex 2043, page 65:7-10. The Example states that 9 grams of azithromycin ethanolate were obtained. Ex 2001, col. 4, lines 5-6. There is no explanation on the record as to why a dry weight—to use the term Dr. Perlman's lab notebook—of only 6.48 grams was obtained by Dr. Perlman while the Example states that 9 grams were obtained. Ex 1106, page 39:-14-17. Nor do we know whether the product not removed is the same as the 6.48 grams of product which was removed.

Any reader of the cross examination deposition transcript of Dr. Perlman cannot help but notice how often she could not remember details about an experiment which at least some Teva personnel would have been expected to know was significant for the case. *See, e.g.*, Ex 2043, page 27:11, page 32:24; page 35:5, 9 and 25; page 36:9; page 38:3; page 39:10-12; page 44:17 and 20; page 46:6; page 53:22-23; page 56:19; page 57:2 and 7. We find it at least curious on re-direct she was able to "remember" that product was left in the reactor after the 6.48 grams was recovered.

One can speculate that the protocol suggests that the product prepared by Dr. Perlman was to be analyzed. Ex 1090, page 6. Dr. Perlman's lab notebook states nothing about analysis to be conducted. It does not state

where samples are to be sent and what analysis is to take place. Likewise, Dr. Perlman's notebook (or at least the portions given to us) does no reflect the results of any analysis. The Example states nothing about whether, or how, its 9 grams of azithromycin was analyzed. Dr. Perlman testified that she had samples sent to Ms. Gultchin (we assume Ms Gultchin is Ayelet Sherman-Gultchin), but did not give it directly to Ms. Gultchin. Ex 2043, page 55:1-21. She also gave a sample to the manager of Maya Cwikel and that "[s]he [, i.e., Maya,] received it" because Dr. Perlman was told so by Sharon Tayer. Ex 2043, page 55:22. The samples to Ms. Gultchin and Ms. Cwikel could have been sent by or one of my team, but "I don't remember exactly." Ex 2043, page 56:2-4. Dr. Perlman also sent a sample to Dr. Claire Grey. According to Dr. Perlman, the sample was given to Sharon Tayer—who is said to work in the patent department of Teva. Apparently Dr. Perlman believes Sharon Tayer sent the same to Dr. Grey, although how it was sent seems to be somewhat up in the air. Ex 2043, page 56:13 through page 57:4. We are unable on this record to determine the precise chain of custody from Dr. Perlman to any of Sherman-Gultchin, Cwikel or Grey. We note that no "sample out logs" from Dr. Perlman's lab or "sample in logs" from any of the testing labs appear in the record. Moreover, we cannot help but wonder whether it can be considered normal practice for a scientist like Dr. Perlman to give a sample to an employee of a patent department for delivery to a testing laboratory.

Credibility findings

(1) The Perlman experiment

We decline, based on the evidence relating to the Perlman experiment, *as a whole*, to credit the results of the experiment. In declining to credit the

Perlman experiment, we wish to make clear that no single factor controlled; rather, all factors mentioned below taken collectively lead us to not credit the Perlman experiment.

First, we note that the Singer Example is not a precise recipe for making a product, leaving a person seeking to reproduce the Example to determine certain times, temperatures and quantities of water to be added at different intervals. Ex 1106, page 42:20 through 43:5. The fact that the Example is not a precise recipe, of course, complicates Singer's attempt to prove that "repeating" the Example will necessarily and inevitably result in a product which is the same as "substantially pure" Form F of Li. In this respect, we note that the Singer patent reveals that varying the process parameters set out at col. 2, lines 38-67 of the Singer patent results in different products being produced. Singer has not shown that varying the parameters of the Singer example likewise will not result in different products. Obviously, if some conditions within the Example result in "substantially pure" Form F and other conditions do not, inherency has not been established. At oral argument, counsel for Singer (Mr. Lee) suggested that one test was enough and that having "successfully" run one test, the burden falls on Li to show a set of conditions were "substantially pure" Form F is not made. Ex 1106, pages 46:2 through 47:7. While it is true that Li could have tried to do so, Li's litigation decision not to do so does not *per se* establish that Singer has met its burden. The problem with Singer's argument is that its own patent shows that varying conditions can result in different products, *e.g.*, Singer Batches A through G. In this particular case, one experiment does not satisfy us that Singer has proved its inherency case.

Second, based on Dr. Perlman's testimony, *as a whole*, we are not comfortable finding that the procedure set out in the Example was faithfully

followed. For example, there is some confusion on the record as to whether ethanol was added to azithromycin or vice versa. We do not know whether it would make a difference.

Third, we know that water was added in various quantities to the Perlman reaction mixture from time to time, but we do not know how much was added and when and whether the manner in which water was added makes a difference. We do not know why 40°C was selected as the drying temperature or whether a precise drying temperature makes a difference.[5] We know that 6.48 grams of material was recovered, that some material was left in the reactor and that the Singer Example speaks in terms of 9 grams of product. We do not know (1) why Dr. Perlman did not recover 9 grams of product, (2) what amount was left in the reactor, (3) whether what was left in the reactor was the same as the product of the 6.48 grams and (4) whether it makes a difference. Ex 1106, page 41:14 through page 42:19.

Fourth, we are not satisfied that Singer has established a proper chain of custody for the samples going to Dr. Perlman to the individuals who made any analysis. Ex 1006, pages 39:14 through 40:7. Whether a chain of custody is sufficient depends on the facts. Sometimes the chain is sufficient and sometimes it is not. In other contexts, *see, e.g.*, *Frank v. Department of Transportation, Federal Aviation Administration*, 35 F.3d 1554 (Fed. Cir. 1994) (chain of custody acceptable) with *Dixon v. Department of Transportation, Federal Aviation Administration*, 8 F.3d 798 (Fed. Cir.

[5] There is some basis in the record for finding that the drying temperature must be below 110°C. According to Li: "The powder samples show a dehydration/desolvation endotherm at an onset temperature of 110-125°C." Ex 2003, page 15, lines 1-3. *See also* Ex 1105, page 32:8-11, where Dr. Meenan testing that his general experience has been if you excessively dry materials or use different drying times, you can potentially damage crystalline materials.

1993) (chain of custody not acceptable). The record does not contain any "sample out logs" from Dr. Perlman's lab or any "sample in logs" arriving at the analysis lab. We recognize that those who made the analysis may have thought they were analyzing NP-P5. We also take note that a sample was said to be transmitted to the analysis lab through an employee of the Teva patent department. Transmitting samples through patent department employees seems somewhat peculiar to us. We are not prepared to find that someone switched a sample, although we recognize that another experiment involving a sample identified as NP-P3 is recorded in Dr. Perlman's lab notebook. Sample NP-P3 also is said to be related to the Singer patent. *See, e.g.*, Ex 2043, page 15:12-13; page 16:17-19 and page 17:11 through page 18:4. It was Singer's burden to establish a chain of custody and it has not done so to our satisfaction.

Fifth, Dr. Perlman often could "not remember" details. To be sure, her first language is not English, but we are satisfied that she ultimately understood questions posed by counsel for Li and that she truthfully could not remember certain details. However, an inability to remember details, particularly during cross examination, does not give us a solid basis for crediting her testimony.

Sixth, Singer had the burden of proof on the necessary and inevitable proof. Any doubts—and we definitely have some doubts—as to whether it met its burden are appropriately resolved against Singer.

We recognize that the evidence we decline to accept might be accepted by someone else as being sufficient to establish what Singer seeks to establish. However, for the reasons given, we believe the Perlman experimental effort is entitled to little, if any, weight on the issue of whether

following the Singer Example necessarily and inevitably leads to production of "substantially pure" Form F as claimed by Li.

(2) Expert witness credibility

We have been assisted considerably by the testimony of Dr. Quallich, Dr. Meenan and Dr. Rogers. However, to the extent there is a conflict between the testimony of Dr. Quallich and Dr. Meenan, on the one hand, and that of Dr. Rogers, on the other hand, we credit the testimony of Dr. Quallich and Dr. Meenan. In our opinion, the testimony and reasoning of Dr. Quallich is more consistent with, and faithful to, the language in the Li and Singer specifications. Dr. Meenan's testimony is consistent with Dr. Quallich's testimony. Our determination of what Li meant by "substantially pure," which is a significant issue before us, is based primarily on the Li specification. Dr. Rogers, in our judgment, placed too much emphasis on Li's original claims, one of which (claim 9) we think was at best an improper claim (Ex 1106, page 18:19-21) and therefore not a reliable basis upon which to determine what Li means by "substantially pure" (Ex 1106, page 19:3-14) Dr. Rogers' reliance on claim 9 may have been justified in his mind given that Singer presented claim 9 along with other evidence to Dr. Rogers for evaluation. However, it does not appear anyone explained to Dr. Rogers why claim 9 may not have been a proper claim.

On the issue of whether the samples identified as Singer Batches A through G were dried to constant weight (assuming they were actually made), we credit Dr. Meenan's testimony over contrary testimony of Dr. Rogers. Ex 1106, pages 13:6 through 14:15. Furthermore, we do not agree as suggested at oral argument that Dr. Rogers and Dr. Meenan agree on constant drying. Ex 1106, page 65:4-11.

We also think that Singer generally, and Dr. Rogers in particular, overlook the fact that Li describes two embodiments related to Form F, *i.e.*, Form F itself (a genus) and "substantially pure" Form F (a subgenus within the genus), but claims only "substantially pure" Form F. Ex 1106, page 17:7-13. We do not know why Li made a point of originally claiming other forms (*e.g.*, Forms D, E and J to name a few) broadly and Form F narrowly other than to speculate that perhaps Li believes on the basis of certain early patents that Form F broadly, but not "substantially pure" Form F, was known. In any event, we focus only on the claims before us.

Singer Responsive Motion 1

In response to Li Motion 1, Singer filed Singer Responsive Motion 1 seeking to add claims 41-43 to the Singer reissue application in the event that the involved Singer patent claims do not interference with the Li claims.

Claim 41 reads (Paper 33, page B-3, ¶ 16):

> 41. A non-hygroscopic ethanolate of azithromycin having an ethanol content of about 2.5%.

Claim 42 reads (Paper 33, pages B-3 and 4, ¶ 42:

> 42. A non-hygroscopic ethanolate of azithromycin having an ethanol content of 2.2% to about 2.5%.

Claim 43, a product-by-process claim, reads (Paper 33, page B-4, ¶ 18):

> 43. A non-hygroscopic ethanolate of azithromycin produced by a process comprising:
>
> a) dissolving 10 g of azithromycin in 30 ml of absolute ethanol in a 0.25 liter three-necked flat flanged jacketed vessel at 20°C;
>
> b) adding 3 ml of water;
>
> c) heating at a constant temperature gradient so as to reach 55°C after 4 hours while adding additional water having a total volume of 11 ml between 35°C and 55°C;
>
> d) maintaining a temperature of 55°C for 2 hours while an additional 49 ml of water is added;
>
> e) cooling to 20°C over 2 hours to form a precipitate; and
>
> f) filtering and drying the precipitate to obtain an ethanolate of azithromycin.

The process of claim 43 is an attempt to claim the process set out in the Example of the Singer patent.

Meaning of "non-hygroscopic"

The parties do not agree on the meaning of "non-hygroscopic" as used in the Singer reissue claims 41-43.

Singer, who has the burden of proof on the issue of whether proposed Singer reissue claims should be added to the interference, argues that "non-

hygroscopic" means "less hygroscopic than azithromycin monohydrate". Paper 54, page 3, last ¶.

The basis for Singer's argument is the Singer reissue application itself. For ease of reference, we refer to the Singer patent and not the specification of the Singer reissue application.

Singer states that the "invention provides a new *non-hygroscopic* form of azithromycin ***." (Emphasis added). Ex 2001, col. 1, lines 37-38.

The Singer patent goes on to discuss a Chinese patent application and a European patent and Singer states that the azithromycin crystal of the Chinese patent is stated to be less hygroscopic than the "dehydrate" described in the European patent. Ex 2001, col. 1, lines 53-56.

According to Singer, the azithromycin obtained by the method of the European patent is "a hygroscopic monohydrate." Ex 2001, col. 1, lines 42-44.

Further according to Singer, "[t]he present invention provides a new ethanolate of azithromycin that is less hygroscopic than azithromycin monohydrate." Ex 2001, col. 1, lines 61-63.

As mentioned earlier in the opinion, Singer Fig. 1 is said to be a comparison of hygroscopicity of the Singer azithromycin ethanolate vis-à-vis that of azithromycin monohydrate "based on data provided in" the European patent. Ex 2001, col. 2, lines 13-16.

Singer tells us that hygroscopicity profiles were obtained by maintaining samples in controlled humidity chambers for a period of two weeks, followed by Karl Fischer analysis of water content. Ex 2001, col. 3, lines 38-40.

Chemists know that a Karl Fischer analysis can be conducted to measure water content so there is no need in this opinion to get into the

details how the analysis is performed. For a brief description of a Karl Fischer analysis, see Ex 1105, page 10:5 through page 11:24.

The Singer patent does not state that the product of its Example was analyzed for water content.

The Singer patent does not state precisely how each of the samples identified as Batches A through G were made for which ethanol and water content analysis are set out in Table 1 on col. 3. We will assume that Karl Fischer analysis was made very shortly after drying because (1) the Singer azithromycins are said to be somewhat hygroscopic (meaning they will pick up some water albeit not as much as azithromycin monohydrate) and (2) unless a sample is analyzed promptly any resulting analysis data would be compromised. Ex 1105, page 48:17-18 and page 49:14-20. However, we cannot find that the samples were dried to constant weight.

The Singer patent does not identify the precise azithromycin ethanolate used to obtain hygroscopic date for Fig. 1 and certainly does not state that the hygroscopic data of Fig. 1 is based on measurements of the azithromycin ethanolate of the Singer Example.

We will assume *arguendo* that the hygroscopic data set out in Fig. 1 for the Singer compound were probably obtained by measuring water content of samples maintained in a controlled humidity chamber for a period of two weeks, recognizing of course that statements in a specification are hearsay. Ex 2001, col. 3, lines 38-40.

Li has called two patents to our attention which define, for the purpose of each patent, the meaning of "non-hygroscopic."

One patent is owned by Pfizer and the other is owned by Teva.

In Pfizer patent 6,583,274 B1, "non-hygroscopic" "when used to describe a composition of matter [in this patent] means the composition of

matter absorbs moisture at a rate of less than about 0.4% over 24 hours at 90% relative humidity." Ex 2046, col. 3, lines 59-62.

In Teva patent 6,696,600 B2, "a non-hygroscopic compound is defined as a compound that absorbs less than 1% water at 80% relative humidity *** for 24 hours ***." Ex 2047, col. 5, lines 37-39.

The Singer, Pfizer and Teva patent "definitions" seem to suggest that there is a need to know (1) an amount of water absorbed, (2) a relative humidity under which a hygroscopicity test is run and (3) a time during which a sample is maintained at the relative humidity.

When the Singer patent is considered as a whole, we find that "non-hygroscopic" means "less hygroscopic than azithromycin monohydrate."

It is true, as pointed out by Li, that Singer Fig. 1 shows that at a relative humidity of about 20%, Singer's azithromycin appears to be more hygroscopic than azithromycin monohydrate. Ex 2001, Fig. 1.

However, except for a small range around 20% relative humidity, Singer's compound is described as being less hygroscopic than azithromycin monohydrate.

Having found a meaning of "non-hygroscopic," however, does not end the matter.

Are Singer's "non-hygroscopic" azithromycins "substantially pure"?

Singer, if it wants to maintain that Singer reissue claims 41-43 interfere-in-fact with Li's claims, then Singer has a burden of establishing that the subject matter of Singer reissue claims 41-43 is the "same patentable invention" as that of the involved Li claims.

The discussion in the specification of the Singer reissue application is not admissible to prove that the Singer Example was carried out and that the

data set out in Table 1 or Fig. 1 is based on particular experimentation, *i.e.*, it is not admissible to prove the truth of statements therein. *See* STANDING ORDER, ¶ 152.2.1 (Jan. 3, 2006) (Paper 15) and *Chen v. Bouchard*, 347 F.3d 1299, 68 USPQ2d 1705 (Fed. Cir. 2003) (board could properly decline to give weight to hearsay notwithstanding the absence of an objection).

Singer maintains that its azithromycin ethanolates have the unexpected property of being "non-hygroscopic."

If so, then Singer has the burden, some would say by clear and convincing evidence, to establish that its azithromycin ethanolates have the property upon which Singer relies.[6]

Singer has not done so under any standard of proof.

Singer presents an argument that non-hygroscopicity" is "an inherent characteristic" of NP-P5 produced by the method of the Singer Example. Paper 54, page 5, lines 20-22.

There are several independent answers to the Singer argument. *First*, we have declined to credit Dr. Perlman's experimental work attempting to repeat the Singer Example. *Second*, even if we were to credit the experimental work, Singer has not shown us where any convincing hygroscopicity analysis was conducted on what Singer identifies as product NP-P5. *Third*, Singer has not established a relationship between Singer's "non-hygroscopicity" and Li's "substantially pure".

[6] *McClain v. Ortmayer*, 141 U.S. 419, 429 (1891) (conclusive evidence needed to establish new function); *In re Klosak*, 455 F.2d 1077, 1080, 173 USPQ 14, 16 (CCPA 1972); *In re Passal*, 426 F.2d 409, 412, 165 USPQ 702, 704 (CCPA 1970); *In re Heyna*, 360 F.2d 222, 228, 149 USPQ 692, 697 (CCPA 1966) (applicant required to submit clear and convincing evidence to support an allegation of unexpected property); *In re Lohr*, 317 F.2d 388, 392, 137 USPQ 548, 550-51 (CCPA 1963).

A difficulty encountered in the case

One difficulty we have had in considering this particular case is the rather nebulous manner in which information has been presented in the Singer patent, particularly in light of Singer's post filing date attempt to pigeon-hole portions of that information into being a description of a "substantially pure" Form F azithromycin claimed by Li.

We do not find or hold that the Singer specification, as a whole, including the Singer Example, is non-enabling as to azithromycin ethanolates which are not "substantially pure" Form F's.

We do not find or hold that Singer failed to provide a written description of azithromycin ethanolates which are not "substantially pure."

Certainly one skilled in the art can make and use the azithromycins described by Singer.

But, Singer has not established that its azithromycin ethanolates are in fact "non-hygroscopic" azithromycins and that if they are, that they are "substantially pure" Form F azithromycins within the meaning of the Li claims.

Recognizing that a specification cannot be admitted in evidence to prove the truth of statements therein, as far as we can tell, there is no admissible or otherwise convincing evidence before us (1) that the hygroscopicity of any Singer azithromycin (e.g., Table 1) was actually measured, (2) that if it was measured, what process parameters were used to make the azithromycin on which any hygroscopicity measurements were made and (3) whether any water content test has been reliably reported given that counsel for Singer (Ms. Moken) made somewhat of a "big deal" during cross examination of Dr. Meenan as to whether Batches A through G may

have picked up water prior to any water content analysis (Ex 1105, page 40:13 through page 46:4.

Likewise, we are not convinced that a "non-hygroscopic" Singer azithromycin ethanolate, such as those recited in Singer reissue claims 41-43, is *per se* "substantially pure" Form F within the meaning of the Li claims.

Lack of anticipation finding

The subject matter of the involved Singer patent claims and of Singer reissue claims, including reissue claims 41, 42 and 43, does not anticipate the subject matter of the involved Li claims.

Obviousness

(1) Scope and content of the prior art

The relevant prior art is the subject matter of the Singer claims, which for the purpose of determining whether an interference-in-fact exists, is presumed to be prior art. In other words, one assumes—subject to the outcome of a priority determination—that Singer's claimed subject matter is prior art under 35 U.S.C. § 102(g) vis-à-vis Li and the patentability analysis proceeds on that basis.

In addition, the Singer patent itself is prior art under 35 U.S.C. § 102(e). Accordingly, the prior art includes Singer's method for making azithromycin ethanolate as described in the Singer patent.

The prior art also includes references identified by Dr. Quallich. Ex 2007, ¶ 41, including azithromycin dihydrate and azithromycin monohydrate.

(2) Differences

The subject matter of the Singer claims differs from the subject matter of the Li claims in that the Singer claims do not describe a "substantially pure" Form F. Rather, taken in a light most favorable to Singer, the Singer claims describe a "genus" of Form F azithromycins. Li, on the other hand, describes—to use Singer's words—a subgenus of "substantially pure" Form F azithromycin.

(3) Level of ordinary skill in the art

We have not received from the parties the help we might have wished for with respect to the level of ordinary skill in the art.

Dr. Quallich states that person having ordinary skill in the art is assumed to be reasonably familiar with making and analyzing crystalline forms of pharmaceutical compounds. Specifically, that person would have a relevant scientific degree, and would have at least about 2-3 years of relevant experience with analysis and characterization of crystalline forms of pharmaceutical compounds. Ex 2007, ¶ 43.

According to Dr. Rogers, a person of ordinary skill in the art would be a person (1) having a Ph.D., master's degree or bachelor's degree in chemistry, medicinal chemistry or a related field with several years of experience in solid state chemistry or (2) a person with equivalent knowledge from experience in the field. The person would also have had knowledge and background on polymorphs of pharmaceuticals, including methods for their preparation. Ex 1097, ¶ 5.

We are at a loss to understand what either party is talking about.

Dr. Quallich does not identify the relevant degree. Dr. Rogers says that the person has a Ph.D., master's degree or bachelor's degree. Which

degree and what difference does it make? *Cf. Argyropoulos v. Swarup*, 56 USPQ2d, 1795, 1807 (Bd. Pat. App. & Int. 2000).

What does a person with "about 2-3 years of relevant experience with analysis and characterization of compounds" (Dr. Rogers) and "several years of experience" (Dr. Quallich) know? Does it make a difference in what laboratory any experience occurred? For example, would a "first" person working 2 years with Dr. Rogers gain the same knowledge as a "second" person working 2 years with Dr. Quallich? While both would receive valuable training, we doubt it would be identical and, in any event, do not know what it would be.

We generally prefer to have parties tell us what the level of ordinary skill in the art is by pointing to specific scientific information, preferably in the form of texts and other documents, which a person would know. For example, a person having ordinary skill in the art would know that Singer's azithromycin ethanolate is made by following the procedure set out in Singer's patent. How an analysis is conducted can be established by reference to standard "analysis" texts. In this sense, some "meat" can be put on the "bones" of Dr. Rogers' statement that one skilled in the art would be able to follow the "methods of their preparation" because the Singer patent describes a procedure which presumably one skilled in the art can follow. And, the procedures described in the patent are concrete information which we can evaluate. Nebulous statement regarding degrees and experience, standing alone, do not help us make appropriate findings with respect to the level of ordinary skill in the art. We recognize that numerous court opinions talk in terms of degrees and years of experience. All we can say is that to the extent that degrees and years of experience *per se* are helpful to the courts, they are not standing alone helpful to us.

We do not believe the record will show that the level of skill was sufficient to have enabled a person having ordinary skill to make the "substantially pure" Form F of Li based on the relevant prior art called to our attention, including the Singer patent.

When one compares the precise method described by Li and the precise method described by Singer differences immediately surface.

For example, Li dissolves azithromycin in ethanol at 50-70°C; Singer dissolves azithromycin in ethanol at 10-80°C, but preferably 20-30°C.

To be sure, there is an overlap in temperatures. But, why would one skilled in the art use a temperature of 50-70°C when practicing Singer's invention when Singer states a preference otherwise? Furthermore, is the level of skill sufficient to find that using high temperature will result in one product (Li's product) while using low temperatures will result in another product (Singer's product)? We think not.

Certainly, we cannot find that one skilled in the art would have known that use of 50-70°C in the Singer process *might* result in "substantially pure" Form F, while other temperatures would not, particularly since it is not apparent that one skilled in the art would have known about "substantially pure" Form F.

In their respective examples, Li uses a temperature of 65-70°C (experimental) and 65-70°C (maybe prophetic), while Singer uses a temperature of 20°C (experimental).

Li cools the azithromycin/ethanol mixture when adding water, while Singer heats the mixture and then cools.

We cannot find that the level of skill was such that a person having ordinary skill in the art—aware of all the relevant prior art mentioned

above—would have wanted to, and if they had wanted to would have known how to, make "substantially pure" Form F within the meaning of the Li claims.

Li, of course, would not be expected to be in a position to provide the relevant knowledge of skill since Li believes Li was the first to make "substantially pure" Form F. In that sense, it was relatively easy for Li to sustain its burden of proving a "negative" fact—what one skilled in the art does not know!

Singer, while not having the burden of proof on the ultimate issue of whether there is an interference-in-fact, does not give us sufficient credible evidence which would undermine or otherwise rebut Li's "proof" of the "negative" fact that those skilled in the art would have known how to make "substantially pure" Form F, recognizing, of course, that we have not accepted Dr. Perlman's experimental work as establishing that following the Singer Example "necessarily" and "inevitably" results in "substantially pure" Form F.

Dr. Quallich testified that he could find no suggestion that the azithromycin ethanolates of Singer would be "substantially pure." Dr. Quallich is someone with skill considerably exceeding that of Singer's and Li's proffered hypothetical person having ordinary skill in the art. If Dr. Quallich was unable to find a suggestion of how to make "substantially pure" Form F in Singer, then it would not make a whole lot of sense to hold that a person of ordinary skill would find that suggestion in the Singer patent.

C. Discussion

In order for an interference-in-fact to exist, the subject matter of Li's claims must anticipate or render obvious (alone or in combination with other prior art) the subject matter of Singer's claims and vice-versa. 37 CFR § 41.203 (2005).[7] Li admits that the subject matter of its claims anticipates the subject matter of Singer's claims.

The two issues become the following.

(1) Has Li established by a preponderance of the evidence that the subject matter of Singer's claims does not anticipate the subject matter of Li's claims?

(2) Has Li established by a preponderance of the evidence that subject matter of Singer's claims, alone or in combination with other relevant prior art, would not have rendered obvious the subject matter of Li's claims?

We hold that Li has sustained its burden as to both issues.

(1) Anticipation

Whether prior art "anticipates" the subject matter of a claim is a question of fact. We have found that the subject matter of the Singer claims, including the subject matter of Singer claims 41, 42 or 43, does not anticipate the subject matter of Li's claims. In large measure our rationale for finding "no anticipation" appears in our findings, including our findings

[7] Li, as have many other interference parties, cites *Eli Lilly and Co. v. Board of Regents of the University of California*, 334 F.3d 1264, 67 USPQ2d 1161 (Fed. Cir. 2003), for the proposition that the Federal Circuit upheld the Director's then definition of an interference-in-fact. Since *Eli Lilly*, the Director has amended the rules to make explicit was an implicit at the time of *Eli Lilly*. While what Li says is true, the rule—not any court or board case—now governs how the Director has defined an interference-in-fact and when the Director is of the opinion that there is an interference. A citation to the rule, rather than any case law (judicial or administrative), is all that is necessary.

with respect to credibility of experts and weight to be given Dr. Perlman's experimental work.

There is a debate between the parties as to whether ethanol content can be used to determine "purity". Singer says that Li, through its witness Quallich is essentially estopped to deny that purity cannot serve as a basis for determining purity. Why? Because in an *ex parte* declaration presented prior to the interference (Ex 2009, pages 4-7—accompanying a FIFTH SUPPLEMENTAL RESPONSE), Dr. Quallich relied on ethanol content percentages to attempt to distinguish Li's products from Singer's products. Accordingly, Singer says Li cannot now have Dr. Quallich take a contrary position.

A penetrating analysis of the Quallich testimony, both before and after the interference, will show he has been remarkably consistent. What Dr. Quallich said *ex parte* was that the ethanol content of Singer Batches A through G (which Dr. Quallich necessarily assumed were actual and scientifically correct) established that azithromycin ethanolates of these batches are *not* substantially pure Form F azithromycins. As we have explained earlier in the opinion, those batches do not have enough ethanol (bound or unbound) to be "substantially pure." Singer, of course, attempts to use ethanol content (e.g., reissue claim 41 which calls for about 2.5% ethanol) to establish purity and therefore establish that the subject matter of claim 41 is "substantially pure" Form F within the meaning of the Li claims. In Singer's view, Dr. Quallich is saying that Singer cannot do that. Ex 2007, ¶ 14. Specifically, Singer seems to be saying: "Wait a minute, you used ethanol content to discuss purity before the examiner and now you have changed your mind when I try to use ethanol content to establish purity." What Singer overlooks, and what is absolutely plain to us, is that in his *ex*

parte affidavit Dr. Quallich was trying to establish scientifically that ethanol content meant the Singer Batches A through G are not substantially pure. It is quite something else to use the ethanol content to establish that an azithromycin is "substantially pure."

Furthermore, the highest ethanol content percentage in Table 1 is 2.3% (Batches B and D). Singer says that is enough for Singer reissue claim 41, which calls for "about 2.5%" ethanol content. Dr. Quallich, of course, never had to discuss "about" 2.5% ethanol content in his *ex parte* declaration because Table 1 does not include a batch with a 2.5% ethanol content. Moreover, use of "about" language to try to show that Singer was in possession of a "substantially pure" Form F is not convincing in this case. It is possible that somewhere within the broad process parameters described by Singer and through a happenstance, there may be an azithromycin ethanolate which might turn out to be a "substantially pure" azithromycin ethanolate. If so, Singer never recognized it until sometime after it filed it application, maybe around the time Singer and Teva first saw Li's published application. The ethanol content percentages in Singer's reissue claims 41-42 do not establish that those claims cover "substantially pure" Form F.

(2) Obviousness

While we have made findings with respect to the three *Graham* factors, we believe the obviousness issue turns, at least in part, on the proposition that Singer has not described in its patent a method for making Li's "substantially pure" Form F. Absent an enabling description in the prior art, it is not possible to prove a case of obviousness within the meaning of 35 U.S.C. § 103. *In re Hoeksema*, 399 F.2d 269, 274, 158 USPQ 596, 601

(CCPA 1968). *See also In re Kumar*, 418 F.3d 1361, 76 USPQ2d 1048 (Fed. Cir. 2005).

Even if we assume, *arguendo*, that the Singer description through all sorts of picking, choosing and guessing could somehow enable the making of Li's "substantially pure" Form F, we are unable to see why one skilled in the art would have known to do so. "Substantially pure" Form F was not known and, as we have found, is not described in Singer, either explicitly or inherently. We agree with Li that a holding that the subject matter of the Singer claims would not have rendered obvious the "substantially pure" Form F's claimed by Li is consistent with the rationale of *In re Doyle*, 327 F.2d 513, 140 USPQ 421 (CCPA 1964). In *Doyle*, a solid, non-hygroscopic 6-APA having a particular chemical structure and melting at about 209-210°C, which was characterized as being substantially pure, was held to be non-obvious over known cruder forms of 6-APA described in a Sakaguich reference. The CCPA held that in none of the art of record did it find even a suggestion of 6-APA in a solid, non-hygroscopic substantially pure form. Likewise, here we are unable to find a necessary suggestion of "substantially pure" Form F.

We have not overlooked Singer's argument in its brief and oral argument (Ex 1006, page 49:6-14) that there is precedent holding, and perhaps establishing a general (but not *per se*) rule, that a range within a range can be considered *prima facie* obvious. *See, e.g., In re Peterson*, 315 F.3d 1325, 1329-30, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003) (a *prima facie* case of obviousness **typically** exists when the ranges of a claimed composition overlap the ranges disclosed in the prior art) (bold added), as well as cases cited in *Peterson*. Each obviousness case must be analyzed on the basis of its specific facts. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18

(1966). *Doyle* shows why the *Peterson* "typical" rule does not apply to the facts of the particular case before us.

(3) Other arguments

We have considered all arguments made and evidence offered by the parties in connection with the two motions. While we may not have addressed every aspect of every anticipation and obviousness argument made by the parties, suffice it to say that we believe that Li established the non-anticipation fact and non-obviousness and that Singer has failed to convincingly rebut Li's proofs.

(4) Disposition

A motion for a judgment of no interference-in-fact raises an issue which the rules characterize as a "threshold issue." 37 CFR § 41.201 (2005). In the context of this case, Singer Responsive Motion 1 also raises a threshold issue because if Li Motion 1 is granted, Singer is given an opportunity to avoid the consequences of the motion by granted by proposing additional claims which may interfere-in-fact.

We will grant Singer Responsive Motion 1 to add its reissue application to the interference. However, we also grant Li Motion 1 for judgment based on no interference-in-fact and we agree with Li that Singer reissue claims 41, 42 and 43 do not interfere-in-fact with any involved Li claim.

In this case, at the time the interference was declared, *ex parte* affidavits in the files of both parties were considered by the administrative patent judge. *See* Paper 3. Obviously, those affidavits had not been subject to cross-examination. Paper 3, Part B, ¶ 18. A review of the affidavits led

the administrative patent judge to credit Singer's affiant over Li's affiant. Following *inter partes* consideration of the evidence, including cross-examination, we reach a contrary position upon consideration of a considerably different record.

D. Order

Upon consideration of Li Motion 1 and Singer Responsive Motion 1, and for the reasons given, it is

ORDERED that Li Motion 1 for a judgment of no interference-in-fact is granted.

FURTHER ORDERED that Singer Responsive Motion 1 is granted to the extent that the Singer reissue application is added to the interference, but is denied to the extent that it would have us hold that there is an interference-in-fact between any reissue claim and any involved Li claim.

FURTHER ORDERED that the issues raised in the remaining motions before us are moot in view of our disposition of Li Motion 1 and Singer Responsive Motion1.

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Senior Administrative Patent Judge

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Paper 72
Entered: November 8, 2006

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE DIRECTOR OF THE
PATENT AND TRADEMARK OFFICE

ZHENG J. **LI**, ANDREW W. TRASK and JOSEPH E. MERTZ,

Junior Party
(Application 10/652,655 and
Application 10/650,252),

v.

CLAUDE **SINGER** and JUDITH ARONHIME,

Senior Party
(Patent 6,365,574 and
Application 10/816,376).

Patent Interference 105,366 (McK)
Technology Center 1600

Before: McKELVEY, *Senior Administrative Patent Judge*, and DELMENDO and LANE, *Administrative Patent Judges*.

McKELVEY, Senior Administrative Patent Judge.

FINAL JUDGMENT
No Interference-in-fact

For the reasons given in the accompanying MEMORANDUM OPINION and ORDER (Decision on Motions) (Paper 71), it is

ORDERED that the interference is terminated on the basis that there is no interference-in-fact.

FURTHER ORDERED a copy of the MEMORANDUM OPINION and ORDER and this JUDGMENT shall be placed in the files of Li application 10/652,655 and 10/650,252, Singer U.S. Patent 6,365,574 and Singer reissue application 10/816,376

FURTHER ORDERED that if there is a settlement agreement between the parties, attention is directed to 35 U.S.C. § 135(c).

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